

Payment, Coercion, and Undue Inducement

October 26, 2005

Neal Dickert

Johns Hopkins School of Medicine and
Bloomberg School of Public Health

Alexis St. Martin

- “The Intrepid Guinea Pig of the Great Lakes”
- In 1822, accidentally shot in the gut and left with a permanent gastric fistula.
- William Beaumont paid him room, board, and \$150 a year for use of his stomach.



<http://www.guineapigzero.com/AlexisStMartin.html>

Walter Reed

- Yellow fever studies in Cuba (1900).
- Intentional exposure.
- Paid \$100 in gold.
- \$100 bonus for successful infection.
- Payable to family in the event of death.



<http://etext.lib.virginia.edu/healthsci/reed/commission.html#vol>

Payment Today

- **“Make \$1,000's... Get paid hundreds weekly in additional cash income, part-time, while relaxing in a million-dollar, get paid research study... Yes, there are thousands of cash paying studies and even free medical care available!”**
- **“Get paid up to \$1,000 weekly for safe sex research?”**

<http://www.rxgetpaid.com>

PROGRAM DIRECTORY	
 Easy Sleep "ZZZ" Research	 Drive Cars Get Paid
 Alcohol • Medical Marijuana Studies	 Plasma • Blood Donation
 Eat and Shop Get Paid	 Health • Weight Loss Studies
 Safe Sex • Condoms • Sperm Donor	 Surrogates • Egg Donors Wanted
 Anxiety • Depression Bi-Polar Treatment	 Look at Email Get Paid
 Free Samples Get Paid	 Tobacco Smokers • Non-Smokers
 Focus Groups • Product Opinions	 Free Health & Dental Care
 Experimental Drugs and Medications	 PreExisting Condition Studies
Advanced Search	

Tensions Today

“Because payment for participation can have coercive or exploitative effects on potential subjects, institutional review boards (IRBs) generally take into consideration the amount and distribution of proposed monetary payments to subjects to ensure that subjects in the study will not be unduly influenced to participate.”

Schonfeld, et al., *IRB*. 2003.

Overview

- State of Payment in the US
- Ethical Concerns
 - Coercion
 - Undue Inducement
 - Exploitation
- Data on Ethical Concerns in Practice
- Recommendations

The Common Rule

“An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence.”

45 *CFR* 46.116

“Payment to research subjects for participation in studies is not considered a benefit, **it is a recruitment incentive...** The IRB should review both the amount of payment and the proposed method and timing of disbursement to **assure that neither are coercive or present undue influence.**”

FDA Information Sheets, 1998

“... the IRB should review both the amount of payment and the proposed method of disbursement to assure that neither entails problems of coercion or undue influence. Such problems might occur, for example, if the entire payment were to be contingent upon completion of the study or if the payment were unusually large. Payments should reflect the degree of risk, inconvenience, or discomfort associated with participation.”

Office of Human Research Protection. *IRB Guidebook*.

Local Guidance (n=31)

	Academic (n=9)	Pharm/ Biotech (n=6)	CROs/ SMOs (n=8)	Indep. IRBs (n=8)
Incentive	4	4	5	5
Time	7	6	6	8
Travel	6	5	5	5
Inconvenience	8	6	6	6
Risk	3	0	1	6

Dickert, Grady, and Emanuel. *Annals of Int Med*. 2002

Payment in the U.S.

- Only 4 of 9 academic institutions surveyed kept track of which studies pay subjects.
 - Average of 23% of protocols at these academic institutions paid subjects.
 - Likely an underestimate.
- Frequency of payment higher at independent IRBs and pharmaceutical companies.
 - “most” and “about 80%”

Dickert, Grady, and Emanuel. *Annals of Int Med.* 2002

Types of Studies Paying Subjects (n=467 studies)

Phase I	26	5.6%
Phase II	58	2.4%
Phase III	100	21.4%
Phase IV	36	7.7%
Physiologic	88	18%
Behavioral	82	17.6%
Other	77	16.5%
<i>Total</i>	467	-

Grady, Dickert, Jawetz, and Emanuel. *Contemp. Clin. Trials*. 2005.

Amount of Money Being Paid (n=467 studies)

< \$100	30.4%
\$100-249	33.6%
\$250-499	21.2%
\$500-999	10.5%
\$>1,000	4.3%
<i>Mean</i>	\$266
<i>Median</i>	\$155

Amounts shown in U.S. dollars

Grady, Dickert, Jawetz, and Emanuel. Contemp. Clin. Trials. 2005.

Payment in the U.S.

- Significant variation within and between institutions in amount of payment for particular procedures, inpatient days, outpatient visits.
- Wide variation in multi-site studies.
- 8/32 institutions had any specific guidance.

Dickert, Grady, and Emanuel. *Annals of Int Med.* 2002.

Grady, Dickert, Jawetz, and Emanuel. *Contemp. Clin. Trials.* 2005.

The State of Payment in the U.S.

- Payment is very common.
- All types of subjects are paid.
- Payment is erratic with little institutional guidance or consistency.
- Payment is generally modest.
- Significant disagreement over payment as incentive or for risk.

Ethical Concerns

- Concerns focus on the enrollment of vulnerable populations.
 - Poor and homeless
 - Sick patients
 - Children and other impaired populations
- Often cast as worries about coercion, undue inducement, and exploitation.

Coercion

“By now it is an unquestioned ethical precept of biomedical and behavioral research practice that subjects should not be coerced into participating... Those who choose to participate in research should be capable of choosing freely; they must do so voluntarily, willingly, without duress, and without being subjected to threats or the promise of too great a reward.”

Macklin, *IRB*. 1981.

Coercion

“... [A] patient suffering from a life-threatening disease may feel as though she has little choice regarding treatment. Physicians should be aware of how vulnerable patients may be to the coercive influence of unrealistic hope, especially those suffering from chronic, life-threatening disorders.”

Berg, Appelbaum, Lidz, and Parker, *Informed Consent: Legal Theory and Clinical Practice*. 2001.

Coercion

- Used in many different circumstances, often incorrectly.
- Often misunderstood as simply meaning involuntary or under strong influence.
- Misused to refer to situations in which there are no good options.
- Because coercion is not a benign accusation, the concept is in need of clarification and should be used carefully.

The Belmont Report

“Coercion occurs when an overt threat of harm is intentionally presented by one person in order to obtain compliance.”

National Commission, 1979

Coercion Requires a Threat

- Classic case- “your money or your life”
- Structure- *A* wants *B* to do *X*. If *B* does not do *X*, *A* will make *B* worse off than *B* was before the interaction.

Wertheimer, *Coercion*. 1987.

- *If B refuses, B will be worse off than if A had never approached him.*
- The problem is that it's made under a threat of harm.

Can Payment be Coercive?

- Payment is an offer and not a threat.
- To be coercive, a subject who refuses must be made worse off than if he or she would have been if never asked.
- The fact that people will predictably accept an offer does not make it coercive.
 - *Example-* \$2,000 to an inmate for a 5-day Phase I study of a new anti-hypertensive.

Coercion is Rare in Research

- Cases where retribution is conceivable.
 - Inmate may receive poor treatment for refusing.
- Perceived coercion is possible.
 - Patient participates in a study run by his PCP because the patient fears his care is contingent on participation.
- Incentives may be involved, but the incentives are not coercive.

Inducement

- Inducements are offers that get people to do things they would not otherwise do.
- Acceptable inducement
 - Higher salaries or other perks for jobs.
 - Giveaways by stores induce us to shop.
- Inducements in research
 - Any activity to encourage participation.
 - Paying for parking.
- What inducements are acceptable?

The Belmont Report

“Undue influence... occurs through an offer of excessive, unwarranted, inappropriate, or improper reward or other overture in order to obtain compliance.”

National Commission, 1979

Undue Inducement

“...monetary inducements may be undue if they alter patients’ decision-making processes such that they do not appropriately consider the risks of participating.”

Halpern, et al., *Arch Intern Med.* 2004

Undue Inducement

“An offer one could not refuse is essentially coercive (or "undue"). Undue inducements may be troublesome because: (1) offers that are too attractive may blind prospective subjects to the risks or impair their ability to exercise proper judgment; and (2) they may prompt subjects to lie or conceal information that, if known, would disqualify them from enrolling -- or continuing -- as participants in a research project.”

Office of Human Research Protection. *IRB Guidebook*.

Undue Inducement

“Payment ... should not be so large as to persuade them to take undue risks or volunteer against their better judgment. Payments or rewards that undermine a person’s capacity to exercise free choice invalidate consent.”

CIOMS, 2002, Guideline 7.

Undue Inducement

- Individuals induced by large amounts of money are acting involuntarily and may be exposed to significant risk.
- They may be blinded to the risks of participation and thus make uninformed decisions.
- They may lie or conceal information.

Undue Inducement

- Undue inducement is the use of an irresistible offer to get subjects to enroll in studies that represent poor judgment and expose them to serious risk of harm.
 - IRBs should not approve studies that expose subjects to serious risk of harm.
 - Enrolling shouldn't represent poor judgment.
 - What are we really worried about?

Emanuel, *J Law Med Ethics*. 2004.

Undue Inducement

- Concern seems misdirected if a study involves no risk.
 - No worry about paying \$500 to ask people about their favorite color or to do a fingerstick blood glucose test.
 - Participating in research is generally safe.
 - If it isn't, the problem is with the IRB and not with the money.

Undue Inducement

- Concerns about voluntariness are counter-intuitive.
 - Why would payment for research compromise voluntariness when it doesn't in other settings?
 - Doing what you *want* is typically thought of as voluntary.

Undue Inducement

- Concerns about consent are misdirected
 - No data to suggest that this happens.
 - If consent is compromised, improve the consent process.
 - It isn't clear that changes in payment are the right solution.

Undue Inducement

- Concerns about subjects hiding information are unknown.
 - Few data to suggest whether and when it happens.
 - Unknown whether the real concern is scientific integrity or subject safety.
 - Largely an empirical question.

Undue Inducement

- Undue inducement is still a concern:
 - Reasonability of risks to different people varies.
 - Non-risk determinants of poor judgment that involve violations of fundamental values or important preferences.

Reasonability of Risk Varies

- Risk tolerance lies on a spectrum from extreme daredevil to extreme caution.
 - IRBs simply cannot, and should not, accommodate the whole range of risk tolerance.
 - But, as studies get riskier, and as payment goes up, it becomes more likely to induce people to take risks that make them very uncomfortable.
- Worry about institutionalizing a practice enticing people to take risks raising real concerns for them.

Non-Risk Determinants of Judgment

- Values other than risk may make people significantly averse to particular studies.
- *Example:* Some people have value-based objections to getting undressed in front of members of the opposite sex. A study paying a lot of money but requiring them to disrobe may lead them to act contrary to those values.
- They may not be *wrong* to override these values or preferences, but it may be worrisome to institutionalize practices encouraging it.

Undue Inducement- The Real Worry

Undue inducement happens in the setting of very attractive offers that lead people to do things to which they would normally have real objections based on risk or other important values or preferences.

- Acting contrary to important values better captures the nature of undue inducement concerns.
- In most cases, risk will be the primary objection but is not the only consideration.

But why is this wrong?

- Worrisome to institutionalize practices that express disregard for human values.
 - Especially in the setting of institution designed primarily to improve health.
- More to respect than just honoring the decisions of capacitated adults.

Is Undue Inducement a Concern?

- Rare in protocols approved by diligent IRBs.
- Can neither be completely dismissed nor completely eliminated.
- A reason for caution at the ends of the spectrum of risk or in settings where subjects likely have values in conflict with the research.
- Not just researchers' or IRBs' responsibility.

Exploitation

- Raised as a concern when paying vulnerable populations
 - Paying the homeless
 - Paying prisoners.
- “An exploitative transaction is one in which A takes unfair advantage of B.”
Wertheimer, Exploitation. 1999.

Exploitation

- Solution- Offer more?
- Hardly satisfies opponents and raises concerns about undue inducement.
- Significant tension exists between concerns about exploitation and undue inducement.

Exploitation and Undue Inducement

“Paying prisoners the same amount that would be paid to nonprisoners may, however, be seen as unduly influential in a setting where inmates can earn only a small fraction of that amount for any other “work” activity. On the other hand, paying prisoners a fraction of what would be paid to nonprisoners can be seen as exploitative.”

Office of Human Research Protection. *IRB Guidebook*.

Exploitation and Undue Inducement

- Issues of exploitation are far from settled. All exploitation not fixed by offering more.
- Figuring out how to fix unfair advantage exploitation will require confronting undue inducement.
- Highlights the importance of clarity on undue inducement as a concern.

Concerns about Justice

- Pay will lead the poor to accept a disproportionate research burden.
 - Empirically unknown- On a broad level, we don't know who participates in research.
- What is the worry if the studies are acceptable?
- Many people enrolling in research see participating as a net benefit and not a net burden.

Concerns about Justice

- The only true fix is to pay people according to existing income or not at all.
 - Unequal pay for the same work also seems to violate justice.
- The real worries are about exploitation, about taking advantage of people who are not well-off, and about issues of undue inducement.

What do the Data Show?

- Motivations of paid subjects
 - Money is important but not the only factor.
 - 50-95% of subjects motivated primarily by money.

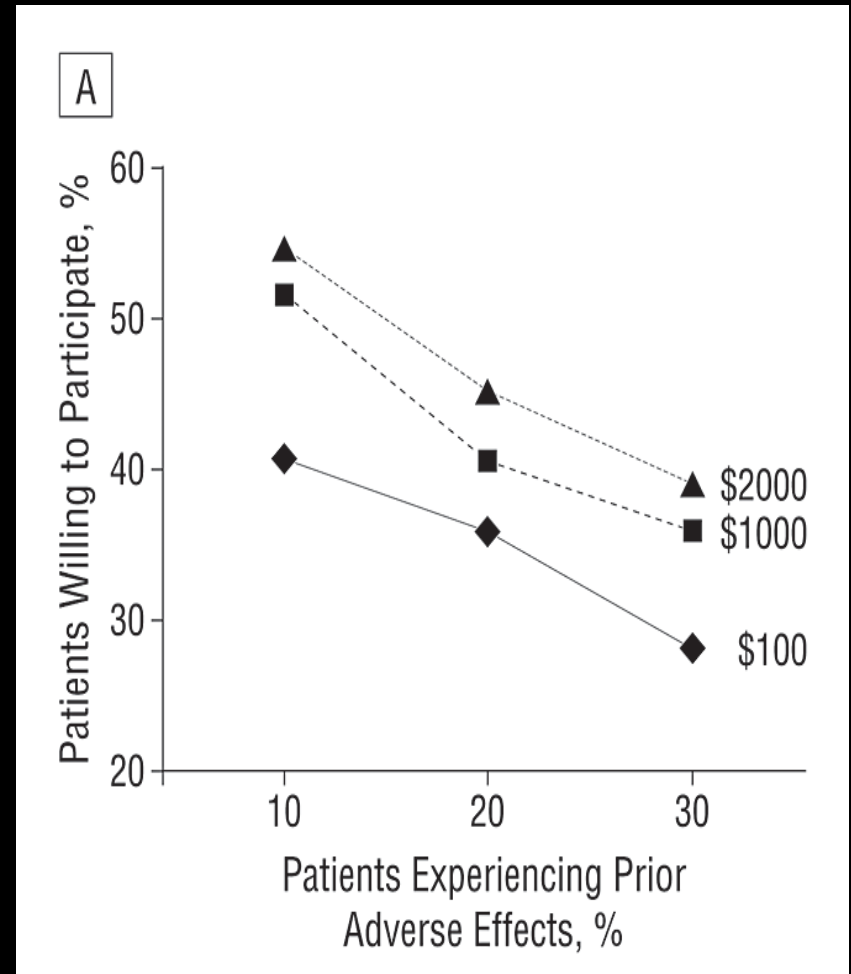
Bigorra and Banos, 1990; Vrhovac, Francetic, and Rotim, 1990; van Gelderen, et al., 1993; Novak, Seckman, and Stewart, 1977; Martin, et al., 1968; Hassar and Weintraub, 1976; Aby, Pheley, and Steinberg, 1996.

- Very little data on the kinds of tradeoffs subjects will make for money.

Influence of Payment on WTP

- Payment influences willingness to participate.
- Influence of payment may level off.
- Relative influence of payment seems stable as risk increases.

Halpern, S. D. et al. *Arch Intern Med.* 2004



Effect of payment on understanding

- No interaction between amount of money and risk rating in hypothetical scenarios.
Bentley and Thacker, J Med Ethics. 2004.
- No data on understanding in actual subjects who are paid versus unpaid.

Summary

- Coercion requires the presence of a threat of harm if a subject refuses participation.
- Undue inducements are very attractive offers that lead people to do something to which they would normally have real objections based on risk or other important values or preferences.
- Exploitation and undue inducement exist in tension.

Recommendations

- More empirical work
 - Tradeoffs people will make for different kinds of offers.
 - Concerns people have about participating in research.
 - Impact of offers on safety and data integrity.
- Focus on the study first, then the offer.
 - Undue inducement is important to consider at the limits of approvability and when fundamental values are known to be stake.

Recommendations

- Clear policies and practices at the institutional and possibly federal level
- Wage payment model
 - Provides consistency.
 - Treats research participation as labor.
 - Allows some incentives and limited protection from undue inducement.